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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,805	STENDER, HENRIK	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-11,25 and 34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-11,25 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to the Amendment and Response filed February 5, 2009. Claims 1, 25 and 34 have been amended, claims 2, 4, 12, and 26-31 have been canceled, and claims 35-37 have been added. Claims 1, 5-11, 25, and 34-37 are now under consideration.

2. The rejection(s) of and objection(s) to claims 2, 4, 12 and 26-31 set forth in the prior Office action of September 10, 2008 are moot in view of the cancellation of those claims. The objection to claim 25 and the rejection of that claim under 35 USC 112, second paragraph are withdrawn in view of applicant's amendments. Additionally, in view of the amendment of independent claims 1, 25 and 34 to require a minimum length of 15 nucleobase subunits, the prior rejections under 35 USC 102(b) and 35 USC 103 relying on the Reeve et al reference have been withdrawn. However, with regard to the remaining rejections under 35 USC 103, applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons given below. It is noted that applicant's amendments necessitated the new grounds of rejection included herein. **This action is FINAL.**

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, second paragraph

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

4. Claims 1, 5-11, 25 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 5-11 are indefinite over the recitation of the limitation "at least 90% identical to the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1 in independent claim 1. The claims do not previously refer to a “nucleobase sequence or complement thereof comprising" SEQ ID NO: 1; accordingly, clear antecedent basis for the recitation “the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1 is lacking. Further, while the claim previously references a “nucleobase sequence,” interpretation of the language noted above as referring back to the previously recited "nucleobase sequence for the detection, identification or quantitation of Pseudomonas" creates confusion, as this nucleobase sequence does not have any specific sequence with respect to which percent identity might be calculated. Accordingly, the manner in which the recitation "at least 90% identical to the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1 in independent claim 1 limits the claims is not clear. The claim should be amended so as to clearly recite the structural requirements of the sequence or sequences with respect to which percent identity is calculated so as to clearly apprise one of ordinary skill in the art as to what types of probes would and would not be embraced by the claims. **For example**, the following language would be considered clear and definite*: ...wherein at least a portion of the probe is at least 90% identical to SEQ ID NO: 1 or the complement thereof.*

Claims 25 is indefinite over the recitation of the limitation "at least 90% identical to the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1. The claim does not previously refer to a “nucleobase sequence or complement thereof comprising" SEQ ID NO: 1; accordingly, clear antecedent basis for the recitation “the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1 is lacking. Further, while the claim previously references a “nucleobase sequence,” interpretation of the language noted above as referring back to the previously recited "nucleobase sequence for the detection, identification or quantitation of Pseudomonas" creates confusion, as this nucleobase sequence does not have any specific sequence with respect to which percent identity might be calculated. Accordingly, the manner in which the recitation "at least 90% identical to the nucleobase sequence or complement thereof comprising" SEQ ID NO: 1 limits the claim is not clear. The claim should be amended so as to clearly recite the structural requirements of the sequence or sequences with respect to which percent identity is calculated so as to clearly apprise one of ordinary skill in the art as to what types of probes would and would not be embraced by the claim. **For example**, the following language would be considered clear and definite*: ...wherein at least a portion of the probe is at least 90% identical to SEQ ID NO: 1 or the complement thereof*.

Claim 36 recites the limitation "the PNA probe of claim 34 for the detection, identification and/or quantification of Pseudomonas" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim, because claim 34 does not recite such a probe; rather, claim 34 refers to a “PNA probe comprising a nucleobase

sequence for the detection, identification or quantitation of Pseudomonas." This rejection could be overcome by amending claim 36 to simply recite, e.g., "the PNA probe of claim 34 and instructions for use".

Claim Rejections - 35 USC § 103

5. Claims 1, 5-7, 9-11, 34-35, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al (Applied and Environmental Microbiology 60(9):3236-3244 [9/1994]) in view of Hyldig-Nielsen et al (US 6,169,169 B1 [01/2001]), for the reasons given below and in the Office action of September 10, 2008. **Applicant's amendments have necessitated the new grounds of rejection included herein, particularly the inclusion of new claims 35 and 37 in this rejection.**

It is noted that the instant claims as amended continue to encompass PNA probes comprising the preferred sequence SEQ ID NO: 1. New claims 35 and 37 specifically recite such a probe. The specification teaches that the sequence SEQ ID NO: 1 is present in each of the Pseudomonas species recited in independent claims 1 and 34 (see, e.g., Table 1).

Ludwig et al disclose 23S rRNA partial sequences for a variety of Pseudomonas species, each of which includes an RNA sequence corresponding to the reverse complement of instant SEQ ID NO: 1 (see entire reference, particularly Figure 2); thus, Ludwig et al inherently disclose that instant SEQ ID NO: 1 exactly complements the 23S rRNA sequence of a variety of pseudomonads. It is also noted that an inspection of Figure 2 of Ludwig et al reveals that there are sequence differences between all pseudomonads and a variety of other bacterial species at the region corresponding to

instant SEQ ID NO: 1 (see Figure 2). Thus, the teachings of Ludwig et al suggest that the region of 23S rRNA corresponding to instant SEQ ID NO: 1 is a suitable target for a genus-specific probe for pseudomonads. However, Ludwig et al do not teach a PNA probe comprising SEQ ID NO: 1.

Hyldig-Nielsen et al disclose PNA probes targeting the 23S rRNA or rDNA sequences of Neisseria gonorrhoeae and Chylamydia trachomatis (see entire reference). Hyldig-Nielsen et al disclose that probe sequences are selected that will hybridize to and identify target organisms of interest (see, e.g., col 4, line 55-col 5, line 24). Hyldig-Nielsen et al further disclose that PNA probes are advantageous as compared to DNA probes for a variety of reasons, e.g., because shorter probes may be used in sensitive assays, because PNA probes "allow greater flexibility in" assay format, and because hybridization can occur "under conditions not favorable for ordinary DNA probes" (see col 2, lines 37-57).

In view of the teachings of Ludwig et al and Hyldig-Nielsen et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have prepared a PNA probe comprising SEQ ID NO: 1 for use in detecting one or multiple Pseudomonas species. As noted above, Ludwig et al disclose that SEQ ID NO: 1 is the exact complement of 23S sequences of a variety of pseudomonads, and that it is not the exact complement of a variety of other species. Hyldig-Nielsen et al suggest selecting such complementary sequences for use in detecting target sequences of interest, and further suggest a variety of advantages of PNA probes as compared to DNA probes. Thus, an ordinary artisan would have been motivated to

have prepared such a probe for the advantage of, and to achieve the predictable result of, preparing a PNA probe that could be used successfully in the specific detection of pseudomonads in a variety of assay formats and hybridization conditions, as suggested by the teachings of Ludwig et al and Hyldig-Nielsen et al. It is also noted that the product suggested by Ludwig et al in view of Hyldig-Nielsen et al could be used by one of skill in the art in a variety of methods “for the detection, identification and/or quantitation of Pseudomonas".

Regarding claims 5-7, Hyldig-Nielsen et al suggest a variety of different labels that may be used successfully with PNA probes (see, e.g., col 8, line 19-col 9, line 57), including, e.g., fluorophores, enzymes, conjugates, haptens, luminescent labels, etc. (see col 8, lines 38-41, teaching multiples labels encompassed by claim 6). With further regard to claim 7, it is a property of many of the labels of Hyldig-Nielsen et al that they may be used in such a way as to be "self-reporting," such that the requirements of the claim are met. (It is noted that the specification teaches at page 9 that beacon probes are simply “examples” of self-indicating probes; thus, the instant claim is not limited to this particular type of self-reporting probe). With regard to claim 9, Hyldig-Nielsen et al also teach unlabeled PNA probes (see, e.g., col 9, line 58-col 10, line 28). Regarding claim 10, Hyldig-Nielsen et al teach PNA probes bound to a solid support (see, e.g., col 19, lines 10-50). Regarding claim 11, Hyldig-Nielsen et al also teach the use of linkers in PNA probes (see, e.g., col 8, lines 19-36 and col 10, lines 29-41).

With regard to new claims 35 and 37, it is again noted that Ludwig et al and Hyldig-Nielsen et al suggest PNA probes comprising SEQ ID NO: 1, which probes are specifically recited by these claims.

With further regard to new claim 37, requiring a PNA probe comprising SEQ ID NO: 1 in a kit, it is noted that Hyldig-Nielsen et al teach kits comprising PNA probes "for use in diagnostics" employing the probes (see, e.g., col 20, lines 1-12). In view of the teachings of Hyldig-Nielsen et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have to have packaged the probes suggested by Ludwig et al and Hyldig-Nielsen et al, including a PNA probe comprising instant SEQ ID NO: 1, in a kit. An ordinary artisan would have been motivated to have made such a modification because Hyldig-Nielsen et al specifically suggests preparing such kits comprising PNA probes "for use in diagnostics."

The response traverses the rejection of September 10, 2008 on the following grounds.

a. First, the reply argues that the Ludwig reference "fails to teach or suggest all the elements of the instant invention," and particularly that Ludwig "does not teach or suggest **a single nucleobase sequence as a suitable target for a genus specific probe** for the detection, identification or quantitation of Pseudomonas". The reply urges that Ludwig et al do not teach or suggest a PNA probe that is "complementary to a target sequence of 23S rRNA or rDNA of the species of the genus of Pseudomonas as instantly claimed." These arguments have been thoroughly considered but are not persuasive. One cannot

show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is noted that the present rejection relies not just on Ludwig et al, but on a combination of references including Ludwig et al. Further, the claims are not drawn to, e.g., a method via which any of the recited species may be identified (i.e., a method that specifically detects the genus Pseudomonas); rather, the claims are drawn to probes having particular properties. As the combined teachings of Ludwig et al and Hyldig-Nielsen et al suggest probes having the structure of applicant's preferred PNA probe (comprising instant SEQ ID NO: 1), the references suggest the invention being claimed. Regarding the issue of complementarity, it is again noted that it is an inherent feature of SEQ ID NO: 1 (i.e., the sequence suggested by the references) that it is complementary to 23S rRNA or rDNA sequences of each species recited in the claims.

b. Next, the reply argues that applicant's have identified a probe that is genus- specific, while the Lugwig reference "nowhere teaches or suggests one specific region of 23s rRNA that is suitable for the detection, identification, or quantitation of Pseudomonas". Applicant further argues that the alignment provided in the Ludwig reference does not suggest "one specific probe that detects one specific region". This argument has also been thoroughly considered but is not persuasive. While the examiner concurs that the alignment provided by Lugwig illustrates more than one region of identity shared by

pseudomonads, this fact would not have dissuaded an ordinary artisan from preparing the probe of the claims; rather, an ordinary artisan would have recognized that multiple regions in the alignments of Ludwig (including that of instant SEQ ID NO: 1) would have been good targets for Pseudomonas detection. While it may have been applicant's goal to identify a single genus-specific probe for Pseudomonas detection, it is not necessary for the prior art to suggest applicant's particular reason for preparing a claimed product - rather, the art must suggest the product itself (as it does in the present case). Further, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

c. Next, the response urges that the "art teaches that no one probe to one specific region of 23s rRNA is known or suggested that can suitably detect, identify or quantitate the genus of Pseudomonas," and that Hyldig-Nielsen et al "(US 6,664,045)" teach that "a set of three probes was required to detect a Pseudomonas genus," referencing Table 1 (col 10)". These arguments have been considered but are not persuasive. Applicant does not provide support for the first statement, and it is not clear where applicant believes such a teaching to be found in either of the references. Further, the patent cited in the rejection is not that referenced in the reply, but is US 6,169,169. The '169 patent, as indicated in the rejection, discloses detection of N. gonorrhoeae and C.

trachomatis using PNA probes designed to detect these organisms. Thus, applicant's argument does not appear to pertain to the present rejection or the references cited therein.

d. The response argues that the Ludwig reference teaches only 4 non-pseudomonads, and asserts that the teachings of Ludwig are insufficient to allow one to determine a region for use as a genus specific probe. This argument has also been considered but is not persuasive. Again, the claims are directed to the probe itself, and therefore do not require that the probe of the claims be employed in a particular way or to achieve a particular goal. The cited references suggest a PNA probe comprising instant SEQ ID NO: 1, and therefore are sufficient to meet the requirements of the rejected claims.

e. Finally, the reply argues that Hyldig-Nielsen et al "does not cure the defects" of Ludwig and does not teach the PNA probes of the claims. However, it is again noted that the instant rejection relies on the combined teachings of the references. Hyldig-Nielsen et al was cited for its teachings with regard to the selection of target sequences for probes, and the advantages of PNA probes over other types. It is unnecessary for Hyldig-Nielsen et al to provide teachings or guidance that were provided by the Ludwig reference.

As the combined teachings of Ludwig et al and Hyldig-Nielsen et al suggest all the limitations of present claims 1, 5-7, 9-11, 34-35, and 37, this rejection is maintained.

6. Claims 7-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al in view of Hyldig-Nielsen et al, and further in view of Gildea et al (US

6,485,901 B1 [26 November 2002; filed 26 October 1998]; cited in the IDS of November 2004]), for the reasons given in the prior Office action of September 10, 2008 and reiterated below.

This rejection applies to claim 7 to the extent that it may be drawn to the particular type of self-reporting probe of claim 8 (i.e., to linear beacon probes).

The teachings of Ludwig et al and Hyldig-Nielsen et al upon which this rejection relies are reiterated above in paragraph 5. While Hyldig-Nielsen et al teach PNA probes labeled at opposite ends with different fluorophores (see, e.g., col 11, lines 26-35), Lugwig et al and Hyldig-Nielsen et al do not specifically suggest PNA linear beacons as set forth in claim 8.

Gildea et al disclose that PNA linear beacons are "particularly well suited" for "detection, identification or quantitation" of target sequences in closed tube assays, asymmetric PCR, and in living or non-living cells, tissues and organisms (because the beacons are not degraded by enzymes) (see entire reference, particularly col 9, lines 31-58). In view of the teachings of Gildea et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the PNA probes suggested by the teachings of Ludwig et al in view of Hyldig-Nielsen et al to have included the donor and acceptor moieties required to form PNA linear beacon probes, as suggested by Gildea et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of preparing a probe well-suited for any of the assays noted above, as specifically suggested by Gildea et al.

The reply traverses the rejection on the same grounds discussed above in paragraph 5 regarding the combination of Ludwig et al and Hyldig-Nielsen et al. Accordingly, the response to those arguments applies equally herein. As the combined teachings of Ludwig et al, Hyldig Nielsen et al and Gildea et al suggest all the limitations of present claims 7-8, this rejection is maintained.

7. Claims 25 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al in view of Hyldig-Nielsen et al, as applied to claims 1, 5-7, 9-11, 34-35, and 37, above, and further in view of Ahern et al, for the reasons given below and in the Office action of September 10, 2008. **Applicant's amendments have necessitated the new grounds of rejection included herein, particularly the inclusion of new claim 36 in this rejection.**

The teachings of Ludwig et al and Hyldig-Nielsen et al upon which this rejection relies are reiterated above in paragraph 5. It is again noted that Hyldig-Nielsen et al teach kits comprising PNA probes "for use in diagnostics" employing the probes (see, e.g., col 20, lines 1-12), such that the combined teachings of Ludwig et al and Hyldig-Nielsen et al suggest kits comprising the probes suggested by the two references. Further, as the kits suggested by Ludwig et al in view of Hyldig-Nielsen et al could be used in any of the assays mentioned in claims 25 and 36 (i.e., for any of the recited intended uses of the probes/kits), the references suggest all of the limitations of the claimed kits with the exception of the "instructions for use" as recited in the claims.

Ahern teaches that premade reagents provided in kit form are convenient and save researchers time and money, and further teaches the inclusion in kits of "detailed

instructions to follow" (see p. 4/6). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the kits suggested by Ludwig et al and Hyldig-Nielsen et al so as to have included therein instructions for use of the enclosed reagents. An ordinary artisan would have been motivated to have made such a modification in order to have allowed an artisan to more readily use the reagents in a correct manner, thereby saving the practitioner time and reagents, as suggested by the teachings of Ahern.

The reply requests withdrawal of the rejection of claim 25 on the grounds that the claim has been canceled. However, the claim was in fact amended and remains pending, such that this argument cannot be considered persuasive. Accordingly, the rejection of claim 25 is maintained, and new claim 36 is rejected for the reasons given above.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571/272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634